Sensory feedback signal derivation from afferent neurons

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QUARTERLY PROGRESS REPORT #4

for the period

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I. Summary of the Overall Project

In this study we are exploring the feasibility of extracting 1) cutaneous sensory information about fingertip contact and slip, and 2) proprioceptive sensory information about wrist or finger position. We use implanted nerve cuff electrodes to record peripheral nerve activity in animal models.

Our overall **objectives** for the 3-year duration of this contract are as follows:

1. Investigate, in cadaver material, implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded.
2. Select a suitable animal preparation in which human nerve dimensions and electrode placement sites can be modeled and tested, with eventual human prosthetic applications in mind.
3. Fabricate nerve cuff electrodes suitable for these purposes, and subcontract the fabrication of nerve cuff electrodes of an alternate design.
4. Investigate the extraction of information about contact and slip from chronically recorded nerve activity using these animal models and electrodes. Specifically,
   a. Devise recording, processing and detection methods to detect contact and slip from recorded neural activity in a restrained animal;
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of functional electrical stimulation (FES);
   c. Record activity for at least 6 months and track changes in neural responses over this time.
5. Supply material for histopathological examination from cuffed nerves and contralateral controls, from chronically implanted animals.
6. Investigate the possibility of extracting information about muscle force and limb position from chronically recorded neural activity.
7. Cooperate with other investigators of the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Summary of our Progress *Prior to* the Fourth Quarter

In the first quarter we completed objective 1 and made progress toward objectives 2 and 3. In three human cadaver arms, we found appropriate implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded. We selected the cat forelimb as the animal preparation in which human nerve dimensions and electrode placement sites are being modeled and tested. We investigated the details of the innervation of the paw and the forelimb musculature in three cats, identified several possible implantation sites, and started to design cuff electrodes suitable for these purposes.

In the second quarter we built 38 nerve cuff electrodes in assorted sizes, suitable for implantation on four nerves in the left forelimb of cats: the proximal median nerve, proximal ulnar nerve, distal median nerve, and distal ulnar nerve (objective 3). We implanted four cuffs in each of three cats, and began to follow the cuff impedance and compound action potential (CAP) properties periodically (objective 4c). We also started to design a forelimb reaching task and the hardware required to extract information about contact and slip from chronically recorded nerve activity (objective 4a, 4b).

In the third quarter we built 22 additional nerve cuffs, completing objective 3 for Year 1. We implanted four cuffs in each of 5 additional cats, completing a series of 8 cats implanted in the first year. We continued to monitor cuff impedance and compound action potential (CAP) properties periodically (objective 4c) in all 8 cats. The first cat in the series was terminated prematurely at 101 days following device failure. We refined the design of the forelimb reaching task, and started the hardware design (objective 4a,b). We started to obtain the equipment required for in-house histopathological examination of cuffed nerves and contralateral control nerves (objective 5).

III. Summary of Progress in the Fourth Quarter

In the fourth quarter we continued to monitor the state of the nerves by measuring cuff impedances and compound action potentials (CAP) periodically in seven implanted cats (objective 4c). Several problems relating to long-term implantation of devices have been encountered and are being analyzed. We carried out post-mortem examination of one cat, and based on these findings we are considering some improvements in nerve cuff design (objective 3). Seven Year 1 cats have been trained with a passive forelimb 2-D manipulator (objective 4a,b), and the 2-D servomotor forelimb reaching task hardware has been re-designed and is being pre-tested for use with the Year 2 cats. A histopathological protocol has been developed to investigate the condition of the nerves and implanted devices in the seven remaining Year 1 cats (objective 5). Finally, developments with a sub-contractor have resulted in a change in direction in nerve cuff development (objectives 3, 7).

IV. Details of Progress in the Fourth Quarter

A. Data collection

During the fourth quarter, we continued with periodic recordings from the 7 remaining Year 1 cats using the protocol described in Progress Report #2. The recorded data are being analyzed to monitor long-term changes in compound action potentials, nerve cuff impedances, and nerve cuff integrity over a minimum 6-month period (objective 4c). The status of Year 1 cats is presented in Table 1.

TABLE 1. Status of implanted cats as of November 30, 1993

Subject	Implant Date	Days implanted (as of Aug. 31)	Status
NIH 1, Dawson	May 10, 1993	101	Terminated on Aug. 19, 1993 Ulnar - cuffs removed after 7 days Median - several cuff leads broken
NIH 2, Pierre	May 19, 1993	195	Ulnar - data OK Median - data OK
NIH 3, Russell	June 2, 1993	181	Ulnar - data OK Median - data OK
NIH 4, Tristan	June 9, 1993	174	Ulnar - data questionable Median - decline in signal amplitudes and then wires broke after day 75
NIH 5, Oliver	July 7, 1993	146	Ulnar - wires broken on day 135 Median - data OK
NIH 6, Victor	July 14, 1993	139	Ulnar - data OK Median - data OK
NIH 7, Samson	July 21, 1993	132	Ulnar - data questionable Median - wires broken on day 39, cuffs removed on day 71
NIH 8, Winnie	Aug. 24, 1993	116	Ulnar - data OK Median - data questionable

The first cat in the series was terminated early, at 101 days, because of evident device failure (discussed in Progress Report #3). The seven remaining cats have been recorded from at regular intervals, with results outlined in Table 1. Unfortunately, several cats have snagged some of their implanted recording device wires (see section B). In some cases, wire breakage has caused the loss of a stimulating or recording point on the nerve. As of November 30, broken wires have prematurely ended recording on 6 out of 16 implanted nerves.

We have observed various changes in the data in three cats which lead us to categorize the data as questionable. The observations include large changes in cuff electrode impedances, nerve stimulation currents, and compound action potential amplitudes. The causes of these deviations will be determined during the acute surgery after day 180. Two of the cats have now come to term and will undergo histopathological examination in December, 1993.

B. Evaluation of long term implantation of recording devices

The problems that we have encountered to date related to long term implantation of devices typically fall into one of three categories: jugular catheter failure, backpack suture infections, and broken wire electrodes. This section briefly discusses the causes and extent of these problems and proposes solutions to address these issues in future implants.

We implanted jugular catheters in our cats to facilitate periodic iv injections of pre-anaesthetic drugs and fluid therapy during surgery. Problems of jugular catheter dysfunction occurred in all subjects after less than 100 days of implantation. In two cases the catheter migrated out of the vein, and in a third case the neck area around the catheter became infected. In each of these three cases, the jugular catheter was surgically removed. In the remaining five subjects, the cause of dysfunction is not yet known but may become evident at the final acute surgery when the devices are removed and inspected. We speculate that these devices have either migrated out of the vein or have become blocked by coagulated blood. Despite a daily flushing regime with 3% heparin solution, blood clots may have formed inside the 1 mm ID silicone tubing.

In order to solve the catheter problems in future implants, we are exploring several alternatives. First, we may insert a longer length of tubing into the jugular vein and secure it more effectively than in the present implants. Second, instead of constructing our own catheters from silicone tubing,.we may begin to use a new type of jugular catheter now available commercially made of tygon tubing and designed specifically for long term implantation. It is smoother and less porous than the silicone tubing we currently use, and comes impregnated with heparin, making its surface less susceptible to clot formation. The third option is to also implant a transcutaneous vascular access port that would replace the port now located in the backpack connector.

The other two problems, backpack suture infections and broken wires, are very closely related and have a significant impact on our data collection in Year 1. In most cats, some signs of infection developed around the transcutaneous exit point of the backpack sutures by day 30 to 40. In some cases, the infection progressed to the point that it invaded the inter-spinal ligaments where the sutures were secured and caused the sutures to move to a subcutaneous position. Despite the fact that the infections were promptly treated with both intravenous and topical antibiotics, they have recurred intermittently throughout the course of the six month implantation. It is thought that the braided Mersilene #2 sutures used to secure the connector act as a wick for possible contaminants to enter the body. These infections not only compromise the well being of the animal, but they also cause the cats to want to scratch in the area of the infection, under the backpack connector. Occasionally, when backpack sutures became loose, they have caught a wire with their claws. To date, data from six out of 16 instrumented nerves has been lost because of pulled and broken wires.

Several possible solutions to these problems are being considered. In future backpack connection applications we will use monofilament sutures instead of braided sutures, to decrease the amount of wicking and so prevent the onset of infection. We are also considering replacing the backpack with a vest that contains a pouch designed to hold the connector and wires in place without the need for anchoring sutures. A third option is to continue to use the current connector configuration but with monofilament suture attachments, and place a full or partial body vest around the cat and the backpack to prevent the cat from snagging wires when scratching.

C. Improved nerve cuff designs

After examining the mechanical and electrical characteristics of our nerve cuffs through periodic recording, and from the post mortem findings in the first cat, we have identified some aspects where the cuff design needs improvement. In Progress Report #3 we presented the post mortem observations of the cuffs after an implantation period of 101 days. Two immediate concerns with

that first implant were that the strain relief of the cuff and wires was inadequate, and that the suture knots used to close the cuff around the nerve during implantation came partially undone during the implantation period. Insufficient strain relief could lead to nerve damage, and the cuff could be displaced along or even off the nerve if the closing sutures came undone. The strain relief problem was addressed in all cats following the first, with longer cuff wires looped subcutaneously and mechanical strain relief built into the cuff itself. In addition, we have been working recently on new cuff closing techniques as shown in Fig. 1.

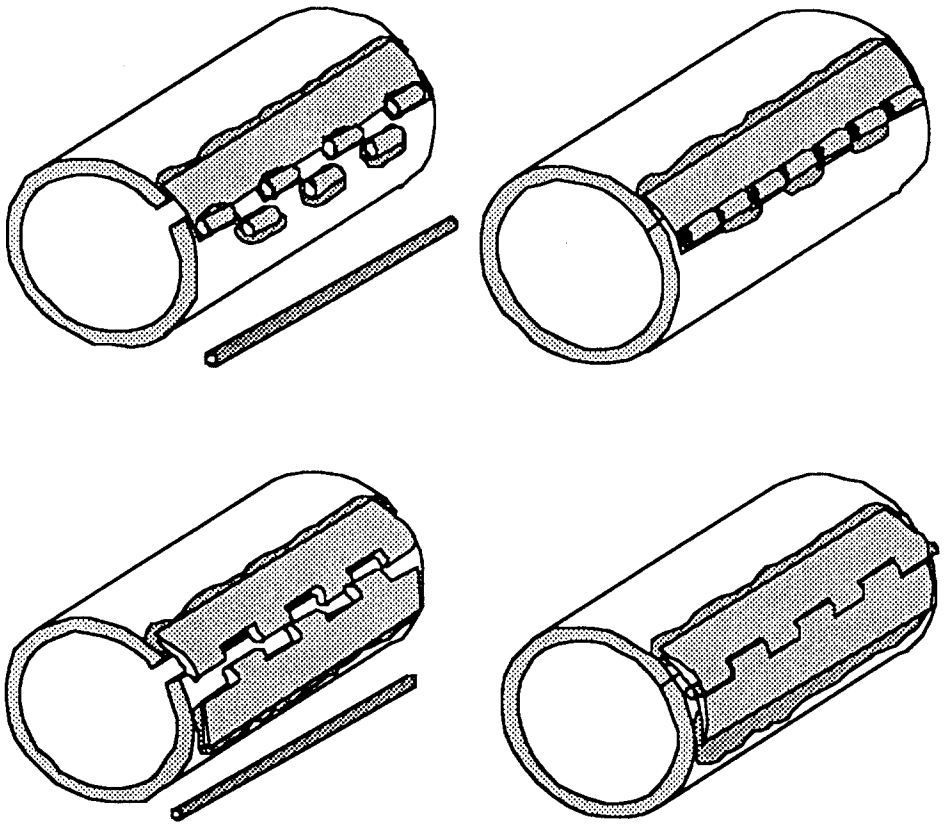


Figure 1: New cuff closing techniques

The top panels in Fig. 1 show a closing technique based on inserting a stainless steel pin through a series of small silicone tubing (0.3 mm ID) segments attached to either edge of the outer cuff wall. The design is more labour intensive to fabricate, but surgical installation time is shortened and the cuff should remain tightly closed for the entire length of the experiment, as sutures are no longer required. The bottom panels present a variation on the first technique with a pin through an interlocking series of loops fabricated from thin silicone sheeting (0.13 mm thick). In our laboratory we are continuously working on cuff design improvements, and several refinements are planned for implementation in the next series of cats (objectives 3, 4a,b).

D. Forelimb task paradigm: conceptual design and development

We are developing a forelimb reaching task designed to elicit voluntary movements in the unrestrained animal (objective 4a). The paradigm is based on a method used by Dr. Kris Horn and collaborators at the Barrow Neurological Institute in Phoenix, AZ to study cat forelimb reaching

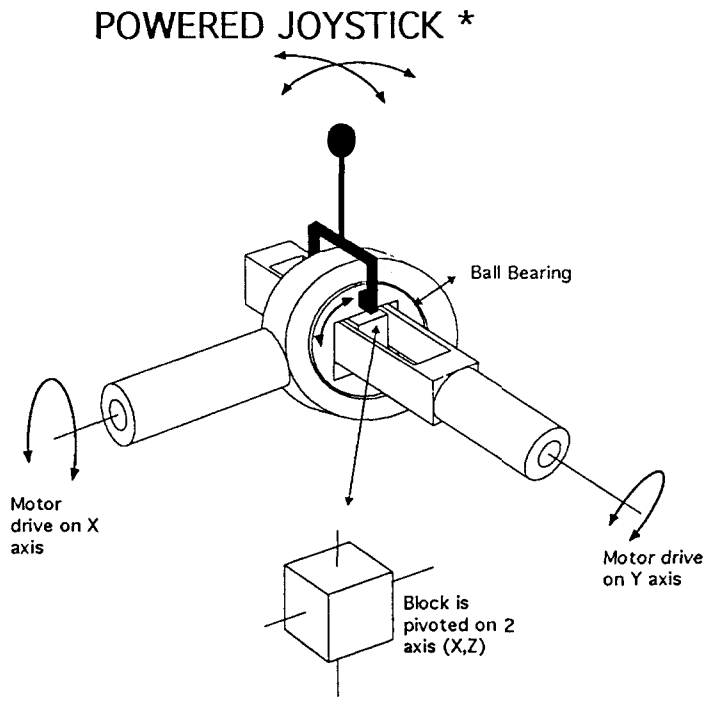
movements during cerebellar recordings (pers. comm.). In our research, we wish to study the natural use of the forelimb musculature during voluntary reaching and manipulations, and record the patterns of sensory nerve activity that occur during such tasks. Reflex and voluntary responses to unexpected perturbations of joystick position or compliance will also be studied in detail. At later stages, we plan to combine sensory nerve recordings with FES of appropriate muscles (objective 4b).

The cats will be trained to, upon hearing a stimulus tone, reach out and pull a joystick in anticipation of a food reward. The joystick drive system will provide an adjustable resistance to the subject's pull. Food rewards will be given on successful completion of a movement task.

A simple model of the joystick was constructed and tested. The subjects took to the task quickly. An unpowered model is now built which includes the food reward system. Training of subjects has begun.

Implementation of the forelimb task consists of three main subsystems:

1) A joystick and electromechanical system to move it (Figure 2):



* Based on an MIT M. Sc. M. E. thesis by Bernard Dov Adelstein

Figure 2: Powered joystick for forelimb reaching task

The current version of the joystick is a hollow tube 20.5 cm long from the point of rotation to the free end. The free end can move in all directions within the limits of a 15 cm circle.

Two DC servo motors (PMI JR16M4CH) will provide motion in two orthogonal directions and allow the generation of 0 to 10 newtons of force at the end of the joystick.

Two switching servo amplifiers (SSA 75-10-30 or AXA 180-10-30) will drive these motors and allow for the possibility of very fast and accurate movements. The 30 Amp peak currents that these amplifiers are capable of will allow the generation of 2 cm perturbations in times of less than 10 milliseconds.

Transducers will measure force on the joystick and position in two directions. The servo motors will be equipped with tachometers for measuring velocity for monitoring and control purposes.

The fabrication of the joystick and motor mounting system has been completed. The servo motors and amplifiers have been ordered and are expected to arrive soon.

2) A pneumatic system to deliver a food reward:

The system is based on the system developed at the Barrow Neurological Institute. Semi-liquid food in a pressurized container is allowed to flow into a cap on the joystick when a reward is desired. The flow is pneumatically controlled (to allow the remote placement of the electrically noisy control solenoids). This system has been prototyped on our training model and seems to work well.

3) Software and a computer to provide control of the above systems:

The software is being written in C using an existing generic menu system. The setup portion of the program will allow the experimenter to specify all parameters related to the generation of motion or response to motion of the joystick, as well as the timing of inter-trial intervals, a stimulus tone and the reward. The control portion of the program will continuously monitor all the parameters and make adjustments in real time. The control program will trigger data acquisition on another computer at the appropriate times. The software is being developed and tested with a single motor borrowed from another project until the proper motors and controllers arrive. Any unanticipated control problems will be modeled with a commercial software package (Simulink by Mathworks).

E. Histolopathological protocol for Year 1 cats

We have developed a histopathological protocol to examine the condition of the nerves and the implanted recording devices after an implantation period of six months (objective 5). A final acute surgery will be performed under deep anesthesia, in which the implantation sites are blunt dissected, the status of the recording sites are evaluated in terms of infections, connective tissue build-up and nerve-cuff integrity, the nerve cuffs are removed, and nerve samples are taken for histological examination of the nerve. Nerve samples will be taken from the contralateral limb for comparative purposes.

The nerve cuffs will be visually evaluated in terms of cuff migration, suture and cuff flap integrity, and electrode wire integrity. In case of a malfunctioning cuff due to broken wires or unknown problems, the cuff will be electrically evaluated to determine the nature and cause of the problem. Broken wires will be located and extended, if possible, to allow stimulation and recording to determine if internal cuff or nerve damage has occurred. If the cuff itself is found to be intact, a data endpoint may be obtained to complete the data set. The nerve cuffs will be stored for further evaluation under a microscope. Intensive nerve cuff evaluation is expected to lead to new insights for improved cuff designs (objectives 3, 4a,b).

The nerve samples will be taken from locations proximal to, below, and distal to each cuff location, as well as from the contralateral limb. The samples will be prepared by embedding in plastic for observation under a light microscope. Details of the planned embedding procedure are as follows:

The fresh tissue samples are immersed in 1/2 strength Karnovsky's Fixative (2 1/2% glutaraldehyde and 2% paraformaldehyde) for a minimum of one hour. The tissue samples are then rinsed in 2 changes of 0.1 M cacodylic buffer, 20 minutes total time. Post fixation in 2% osmium tetroxide (in 0.1 M cacodylic buffer) is carried out for four hours. Then after another rinse in buffer, the tissue is put through gradient dehydration in ethyl alcohol (50, 70, 85, 95 and 100% ; 20 minutes for each alcohol grade). The alcohol is displaced by two, 7-minute rinses in propylene oxide. The samples are then placed in a 2:1 mixture of epoxy resin and propylene oxide overnight . This mixture is replaced with 100% resin for four hours. The epoxy resin mixture consists of 28 grams Poly/Bed 812, 17 grams DDSA, 10 grams NMA; then after these are well mixed, the 0.8 ml of DMP-30 catalyst is added. Polymerization is carried out in a 60*C oven for a total of 40-48 hours. Eight to ten μm thick sections are now cut and stained in a 2:1 mixture of Richardson's Stain and toluidine blue for light microscopy.

During the fifth quarter we will perform the histopathological examination of each Year 1 cat and provide samples for examination by others (objective 5).

V. Progress of Subcontractors in the Fourth Quarter

In the fourth quarter, one of the two Sub-Contractors for this project, Dr. Jerry Loeb from Queen's U., completed an analysis of approaches to construct thin-film, self-spiralling electrodes. Dr. Loeb has concluded that at this time it is not possible for them to produce thin-film, self-spiralling nerve cuff electrodes of the general type described in the technical proposal that led to this Sub-Contract. Furthermore, Dr. Loeb has concluded that self-spiralling electrodes are perhaps not a desirable design to aim for, after all. As an alternative, Dr. Loeb is now favoring a simple electrode design consisting of a "conventional" silicone cuff with Cooner-wire electrodes embedded in the cuff walls. Dr. Loeb provides a description of his findings and his new cuff design in this Fourth QPR, which is reproduced verbatum at the end of this report.

Our research team at SFU appreciates Dr. Loeb's valuable efforts at trying to make this sub-contracted project work over the past year, and regret that it has proven to be unfeasible. We thank Dr. Loeb for providing in his Third and Fourth Progress Reports a careful assessment of the difficulties encountered with the construction of self-spiralling electrodes with thin film electrode deposition substrates. Based on Dr. Loeb's conclusion that the materials for thin film electrodes that were available were not appropriately matched to the requirements for flexible, self spiralling nerve cuff electrodes, we support the decision to discontinue this specific project.

The primary objetives of this contract are to obtain reliable data from peripheral nerves over long-term, and to analyze the properties of nerve signals. The unavailability of self-spiralling electrodes with demonstrated recording reliability means that for next year's implantations, which are scheduled to take place in the Fifth and Sixth Quarters, we will again implant conventional cuff electrodes fabricated at SFU in all our Year 2 cats, as we did with the Year 1 series. We do remain interested in considering other possible sources of thin-film self-spiralling cuffs, if such emerge.

I. Plans for Year Two

In the second year of this contract we intend to:

1. complete the data collection and analysis of cats implanted in Year 1
2. work on cuff design improvements, in-house and through collaborations
3. implant cuffs on forelimb proprioceptive nerves as well as cutaneous nerves
4. develop the 2-D forelimb reaching task paradigm
5. develop a closed-loop FES controller for the forelimb, using sensory feedback

VII. Plans for Fifth Quarter

In the fifth quarter we intend to:

1. complete monitoring the status of Year 1 implanted nerves and electrodes for at least six months per cat (objective 4c)
2. train Year 1 cats on a forelimb reaching task and record data during this task (objective 4a,b)
3. perform histopathological examination of Year 1 cats (objective 5)
4. evaluate results from Year 1 recordings and histopathological examinations (objectives 4, 5)
5. design Year 2 training, implant and recording protocols (objective 4)
6. begin training Year 2 cats on treadmill and forelimb task
7. complete the construction of hardware for the reaching task (objective 4a,b)
8. continue designing improved nerve cuffs and fabrication techniques (objective 3)

Text for QPR #4 from Queen's University Subcontract

Summary

We have been engaged in the design, fabrication and testing of a "self-spiralling, thin-film nerve-cuff electrode". In the previous QPR, we presented an analysis of the design problems related to a chronic recording electrode, concluding that the spiral form was difficult to produce and implant and not particularly desirable biophysically. In this QPR, we summarize our experience with thin-film substrate materials; we conclude that they are intrinsically poor choices. We discuss test results from chronic implants in cats (funded by the Canadian Medical Research Council), comparing the various self-spiralling, thin-film designs with an improved but basically classical design using stranded wire and silicone rubber. Based on the clearly superior manufacturability and biological performance of the latter design, we recommend that our effort to build a self-spiralling, thin-film nerve-cuff electrode be terminated.

Experience with Thin-Film Substrates

Over the course of the past two years, several different wafer runs were completed at Carleton University according to our specifications. These included various thicknesses and curing cycles for polyimide, polyesterimide and laminates of the two, incorporating various metallization patterns for electrodes, leads and lands made from sputtered platinum over titanium. After tinkering with the various process parameters, it was possible to get high quality, tightly adherent metallization that withstood implantation and occasional electrical stimulation in the body, even when the mechanical integrity of the substrate polymer had been severely compromised (see below). The following persistent problems were experienced:

- These polymers are all hard, brittle materials that have relatively sharp edges. Where these edges come into contact with tissue, they tend to produce severe mechanical damage and secondary foreign body reactions. Along large flat surfaces of the material, the foreign body reaction is minimal, consisting of a few microns thickness of unreactive, nonadherent connective tissue with no signs of chemical irritation.
- When the thin-film material is made thinner, it flexes more freely in tissue, but the edges are even sharper and the tensile strength is greatly reduced.
- All exposed edges of the thin-film substrate can be protected by further lamination on silicone rubber, although this substantially complicates the fabrication of completed electrodes. Adhesion to both Silastic Medical Adhesive A and MDX-4-4210 tended to be poor and failed rapidly in vivo. With self-spiralling designs, particular problems were experienced at the internal longitudinal edge of the cuff, which tended to dig into the nerve, causing severe damage.
- The limited length of thin-film lead available on a wafer forces the design to include an enlarged land region for transition from the thin-film conductors to conventional, stranded wire leads for routing through the body to remote, external connectors. The thin-film metallization was sufficiently robust to permit simple soldering, using Medical

Adhesive A overcoating for short-term experiments (weeks); we successfully developed conductive versions of Medical Adhesive A employing platinum and gold powder filling to replace solder for long-term implants. However, the connection region poses a fixation and tethering problem in the worst possible place, usually on a muscle that moves relative to the adjacent nerve.

- Polyimide tended to absorb water, becoming soft and friable after weeks to months. We experienced breakage across the thin leads as they approached the expanded cuff and land areas and at the edges of electrode contacts where the polyimide changes from a thickness of two layers to one layer (where the contact is exposed). Surprisingly, any metallization at the edges of these fractures was still tightly adherent.
- Polyesterimide (and probably also polyimide) appears to be subject to a catastrophic failure mode that we first reported 16 years ago for polyester (Mylar) films in vivo (Loeb et al., J. Biomed. Mater. Res. 11:195-210, 1977). Where the material is stressed, even slightly, it tends to spontaneously fracture, with a sharp, sometimes zig-zag edge that propagates across the width of the film. The unstressed material immediately adjacent to the stressed region retains its normally high tensile strength and metal film adhesion. Similar chronic stresses on dry material produce no apparent damage. The loss of continuity in vivo was not attributable to transient exposure to high stresses exceeding normal tensile limits because we could track the progress of these cracks across the lead regions over several days by following the progressive loss of continuity to and consequent jumps in impedances of individual electrode contacts. Post mortem examination revealed cracks concentrated at the regions of leads where they were flexed over the silicone laminations in a manner that imposed slight tensile stresses on the polyesterimide. We speculate that the chronic tensile stress in combination with water produces an accelerated hydrolytic attack on the polymer; once weakened at one point, the focussing of the remaining stresses in the film at the edges of the weak point leads to rapid propagation of the failure across the film.

It seems unlikely that any materials in this family of polyesters and polyimides will be suitable for chronic in vivo use. Reports on the mechanical integrity of silicone rubber metallized by ion implantation are not encouraging; it seems unlikely that sufficient conductivity can be achieved to permit long, narrow leads on such an elastic substrate. Thin-film metallization of Teflon sounds more promising mechanically but achieving high adhesion to laminations, particularly prestressed laminations required for self-spiralling designs, will be problematic.

In general, if a material has a high enough tensile strength to prevent cracking of a cohesive layer of metallization during normal flexing, then it will probably have sharp, mechanically damaging edges. If a material is highly compliant, then the metallization must be distributed noncohesively in the matrix of the substrate material rather than layered on top, posing problems of achieving adequate conductivity with a low density of conductive atoms.

Experience with Wire and Rubber Nerve Cuffs

If we were primarily materials scientists, we might be tempted to pursue this problem further. However, the strength of our approach was the integration of design, fabrication, surgical implantation and physiological testing in a single team. This allowed us to focus quickly on the real problems and to conclude that our approach was fundamentally unsound. This suggested that our resources would be better redirected to reexamination of nerve cuff designs based on traditional biomaterials, which would also provide a benchmark with which to compare our unfavorable experiences with thin-film designs.

Figure 1 shows the design and fabrication of an improved nerve cuff based on conventional Teflon-insulated, stranded stainless steel wire (Cooner ASW-631) and silicone rubber (Dow Corning Silastic MDX-4-4210). Normally, the multiple leads are sewn into the inner wall of preformed silicone tubing, a tedious process that produces poorly controlled contact spacing and exposure and may leave protruding wire strands that guillotine the nerve. We used a mandrel equal to the desired inner diameter of the cuff and wrapped the bared ends of the wire around the mandrel to form circumferential contacts, affixed with a thin coating of polyvinyl alcohol, a water-soluble adhesive. We then formed the cuff by dipping the mandrel and leads in the unpolymerized silicone and cured it in place, incorporating the leads into the longitudinal axis of the cylindrical shell. The silicone shell is slit longitudinally where the ends of the contacts almost meet, permitting the completed cuff to be slid off the mandrel as the adhesive is dissolved in water. The stranded wires forming each contact are completely exposed, producing a low contact impedance, but they are trapped in pockets in the side wall where the polyvinyl alcohol has been dissolved away.

Conventional ties for cuff opening and closure could be incorporated in the side walls. However, we are experimenting with a variant on the self-spiralling design in which a second piece of thin-wall silicone tubing, without electrodes, is wrapped over the cuff, locating the slits in each tube on opposite sides of the nerve. Relative to a spiral, this design provides the same ability to self-size and to restrict lateral entry of connective tissue by the forceful and extended apposition of two layers of silicone rubber, although the overlap region is restricted to half the circumference.

One animal was implanted with the first set of six such tripolar cuff electrodes, including two 3 mm cuffs on the two sciatic nerves bilaterally and four 1 mm cuffs on the two superficial peroneal and sural nerves. The animal is now three weeks post-implantation and will be sacrificed shortly for histology. The surgery went remarkably smoothly. The slightly undersized cuffs slipped easily over the nerves, requiring only gentle pressure to fall through the slit into the interior; a special surgical handling tool like a miniature rib-spreader was built but was unnecessary in the event. The 3 mm over-cuffs also slipped on easily but the 1 mm ones had somewhat uneven and too thick a wall thickness to hold as securely as desired.

Post-operatively, the electrical impedances of all leads followed a similar pattern of fluctuations associated with resorption of air bubbles, accumulation of edema and eventual scarring in to stable values of around 2-6 kilohms depending on calibre. Tripolar recordings from all six sites (including sciatic) in the quiescent animal provided readily

audible activity associated with light cutaneous stimuli. In the case of both superficial peroneal nerves, sharply modulated bursts of 15 uV riding on 5 uV of background amplifier noise were recorded during normal locomotion (see Figure 2), with virtually no interference from EMG in the first few days despite only modest filtering (1 kHz high pass, 6 dB/octave). Increasing EMG interference was noted after a few days, presumably because of slight ingrowth of connective tissue under the poorly fitting over-cuffs. Thresholds for electrical stimulation on all four cutaneous nerves (as measured by averaging evoked potentials from the corresponding sciatic cuffs) were 20-30 uA for 100 us/phase biphasic squarewaves, with little change between the first and 20th post-operative day. Growth of evoked amplitudes was remarkably crisp for stimuli above threshold, even for sural nerve stimulation. The sciatic nerve recordings continued to be free enough from EMG cross-talk from the adjacent thigh muscles that we were able to monitor stimulus-evoked potentials in a freely walking cat without averaging.

With a tiny fraction of the effort expended on the unsuccessful development of self-spiralling, thin-film nerve cuffs, we were able to develop a readily manufacturable, easily implantable, highly reliable and electrophysiologically effective nerve-cuff based on traditional materials. We expect that a bit more tinkering with the processes will resolve any remaining shortcomings, particularly in the over-cuff concept. It remains to be seen if any self-sizing seal will prove to exclude connective tissue ingrowth sufficiently to permit long-term recording of naturally evoked somatosensory nerve activity during vigorous use of adjacent muscles, particularly without extensive filtering and signal processing.

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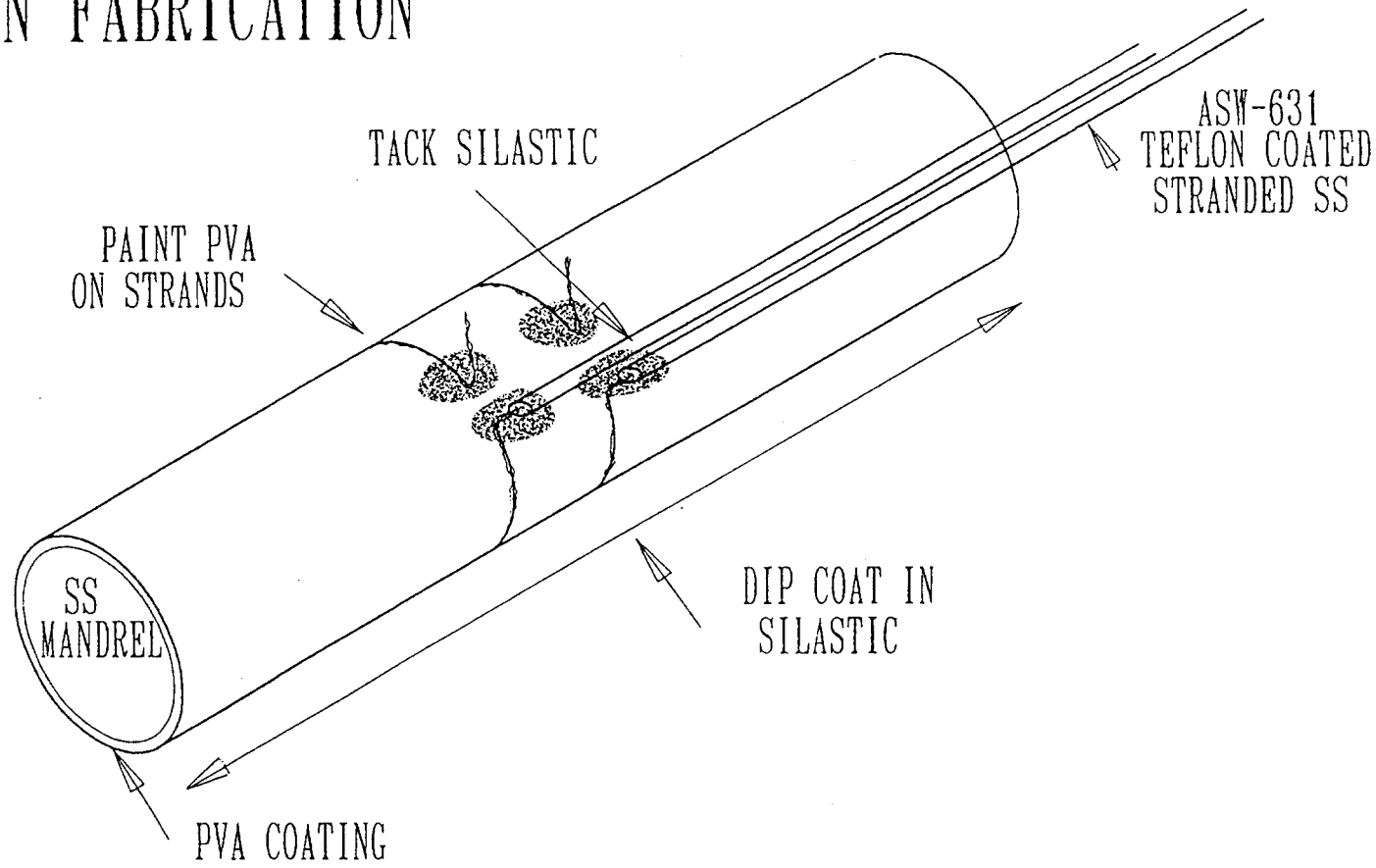

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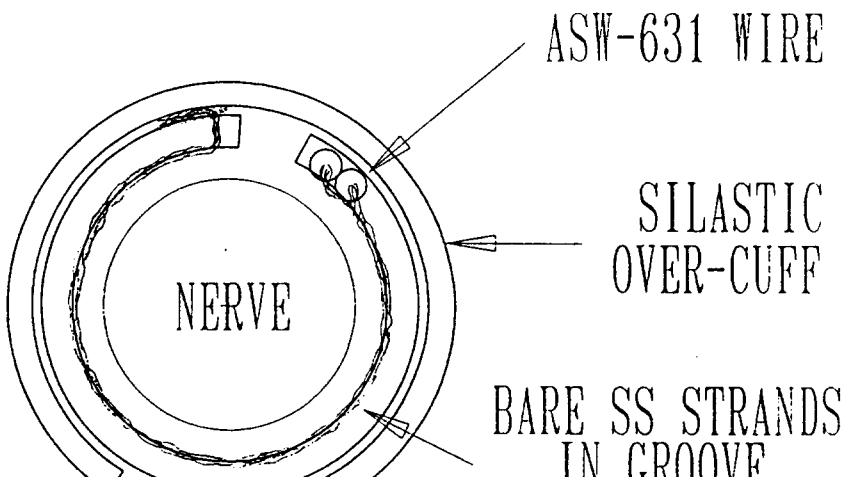

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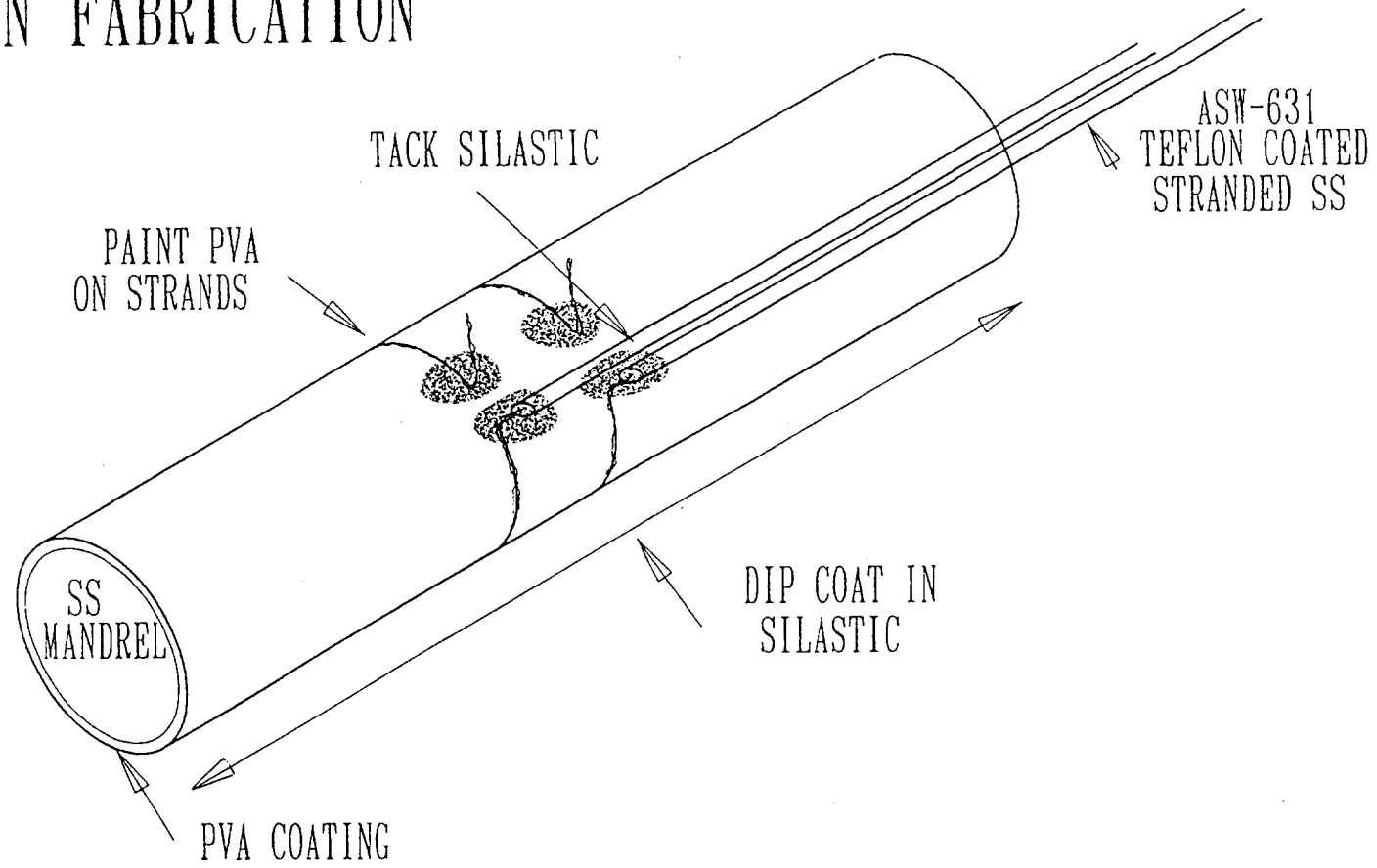
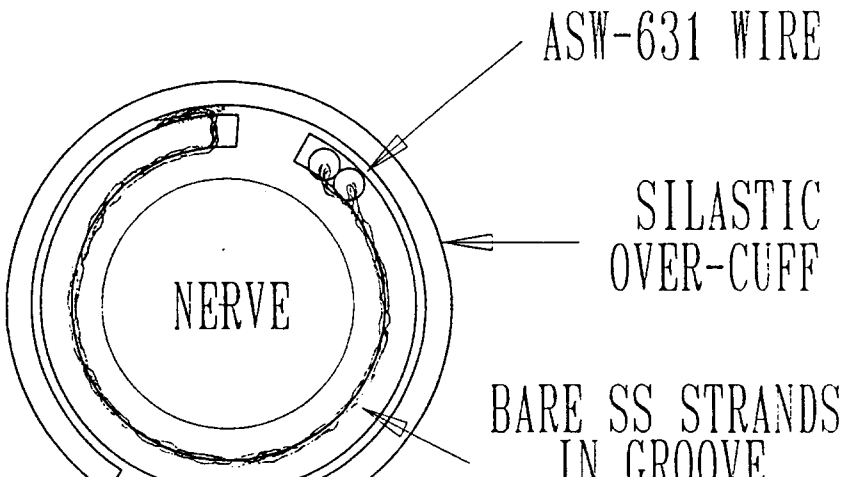


B: IN SITU



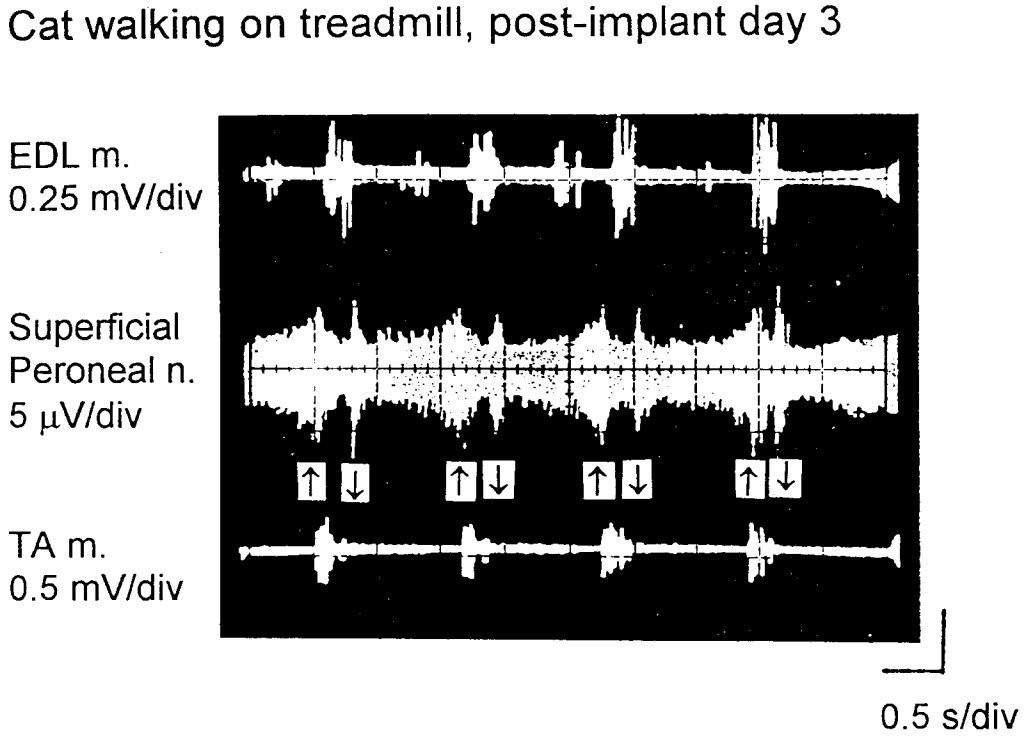
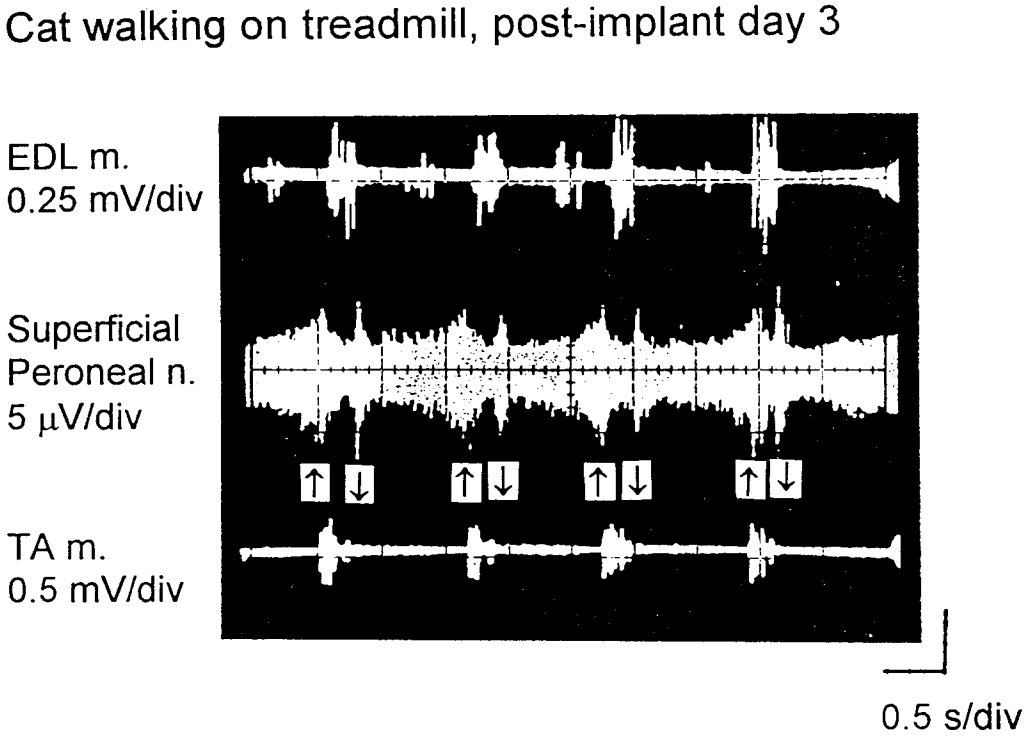


Figure 2: Recordings of multiunit afferent activity in superficial peroneal nerve associated with footfall (↓) and foot lift (↑); obtained from discrete-wire tripolar nerve-cuff electrode (transformer-coupled preamplifier, 1-10 kHz bandwidth over-all, single pole filtering) implanted in an intact, freely walking cat. Note absence of cross-talk from large, phasic EMG signals recorded by epimysial patch electrodes on the two, largest muscles adjacent to the nerve recording site, extensor digitorum longus (EDL) and tibialis anterior (TA).



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